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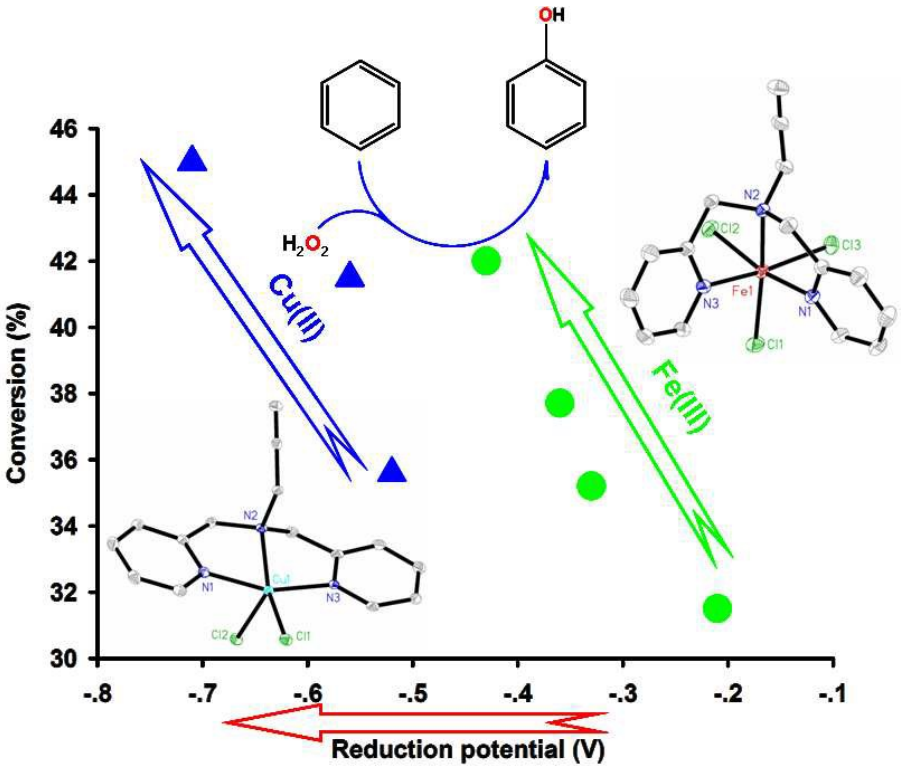
Graphical Abstract

Synthesis and characterization of copper (II) complexes with multidentate ligands as catalysts for the direct hydroxylation of benzene to phenol

Li Wu[a], Wei Zhong[b], Beibei Xu[a], Zhenhong Wei[a], Xiaoming Liu[a,b] *



Like the iron(III) complexes, the copper(II) complexes catalyse the direct hydroxylation of benzene into phenol with H_2O_2 as the oxidant and their catalytic efficiency correlates to the reduction potentials of the copper(II) complexes.

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ARTICLE TYPE

Synthesis and characterization of copper (II) complexes with multidentate ligands as catalysts for the direct hydroxylation of benzene to phenol

Li Wu,[a] Wei Zhong,[b] Beibei Xu,[a] Zhenhong Wei[a] and Xiaoming Liu[a,b] *

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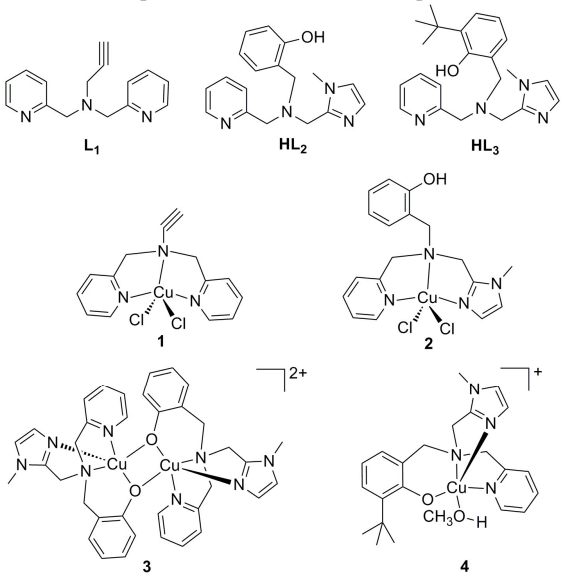
Four copper (II) complexes with multidentate ligands, **1** ([Cu$\mathbf{L_1}$Cl$_2$]), **2** ([Cu($\mathbf{HL_2}$)Cl$_2$]), **3** ([Cu$_2$($\mathbf{L_2}$)$_2$](ClO$_4$)$_2$) and **4** ([Cu$\mathbf{L_3}$(HOCH$_3$)ClO$_4$]) {$\mathbf{L_1}$ = N,N-bis((pyridin-2-yl)methyl) prop-2-yn-1-amine, $\mathbf{HL_2}$ = 2-((((1-methyl-1H-imidazol-2-yl)methyl)(pyridin-2-ylmethyl) amino)methyl)phenol and $\mathbf{HL_3}$ = 2-((((1-methyl-1H-imidazol-2-yl)methyl) (pyridin-2-ylmethyl)amino)methyl)-2-*t*-butyl-phenol} are reported. The complexes were characterized by UV–vis spectroscopy, elemental analysis and electrochemistry. Complexes **1** and **3** were further characterized by X-ray single crystal diffraction analysis. The catalytic performances of these complexes were evaluated on the direct hydroxylation of benzene to phenol with hydrogen peroxide as an oxidant in aqueous acetonitrile media. Under optimized reaction conditions, complex **4** of the most negative reduction potential exhibited the highest conversion without considering the di-nuclear complex **3**. A correlation between the catalytic efficiency and the reduction potentials of these complexes was observed, that is, the more negative the reduction potential, the higher the benzene conversion. A radical mechanism for the catalysis was confirmed by that addition of radical scavengers such as TEMPO into the reaction could severely suppress the catalysis.

1. Introduction

Like iron, copper has been considered as one of the important transition metals in the post-anaerobic evolution of nature and exists in a large number of enzymes.[1-4] It functions as an oxygen transporter in some invertebrates and is involved in electron transportation in respiratory chain. It plays also catalytic role in metabolisms in many organisms, for example, oxygenation of a wide range of organic substrates involving O_2 activation,[5-7] reduction of oxides of nitrogen.[8] P450, one of the *cytochromes*, possesses both mono- and di-nuclear copper centres and plays the role of detoxification in our bodies by degrading a variety of compounds.[9] Copper-containing enzymes play also vital roles in global carbon cycle. pMMO (particulate methane monooxygenase) is such an enzyme found in methanotrophs.[3] This enzyme is responsible for the oxidation of methane to methanol by O_2 in the methane metabolic pathways. The activation of strong C–H bond (438.8 kJ mol^{-1}) is remarkable and inspiring!

In those copper enzymes, the coordination chemistry of the copper centres is satisfied by the ligands (usually amino acid residues of proteins) of N, O, S ligating atoms. Finely tuned electronic and structural properties alongside with the proximal environment offered by protein domains render the enzymes specific functionalities. The coordination chemistry of the copper enzymes has greatly inspired synthetic chemists and exploring the catalytic function of copper complexes has been one of the main research themes in copper chemistry in the past decades.[1, 2, 10-12] Indeed, a great deal of copper complexes, either mono- or multi-nuclear, exhibited functionalities of catalysis on activation of C–H bond of both aliphatic[13, 14] and aromatic compounds.[15]



Scheme 1 Pro-ligands ($\mathbf{L_1}$, $\mathbf{HL_2}$ and $\mathbf{HL_3}$) and their copper complexes **1**–**4**.

Considering the importance of phenol in industry and the drawbacks of the currently employed three-step cumene process, extensive efforts have been made to develop a one-step hydroxylation process of benzene to phenol using either

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heterogeneous or homogeneous catalysts.[16-18] We have been also interested in exploring the catalytic chemistry of base metals complexes on the hydroxylation of benzene to phenol such as iron and copper.[19, 20] Recently, we reported the catalytic performances of iron (III) complexes with multidentate pyridinyl ligand in direct hydroxylation of benzene to phenol.[19] The results showed that the reactivity of the complexes correlates well to their reduction potentials and the conversion was about 40%. The finding suggests that the conversion could be improved by appropriately designing the ligands and thus tuning the electronic effect of the metal centre. As a continuation of our effort devoted to developing homogenous catalysts derived from base metals in the direct hydroxylation of benzene, herein, we report the synthesis, characterization of copper complexes with ligands $\mathbf{L_1}$, $\mathbf{HL_2}$, $\mathbf{HL_3}$, respectively and their catalysis on the hydroxylation of benzene, where $\mathbf{L_1}$ = N,N-bis((pyridin-2-yl)methyl)prop-2-yn-1-amine, $\mathbf{HL_2}$ = 2-((((1-methyl-1H-imidazol-2-yl)methyl)(pyridin-2-ylmethyl)amino)methyl)phenol and $\mathbf{HL_3}$ = 2-((((1-methyl-1H-imidazol-2-yl)methyl)(pyridin-2-ylmethyl)amino)methyl)-2-*t*-butyl-phenol (Scheme 1). Among the four complexes, $[Cu\mathbf{L_1}Cl_2]$ (**1**), $[Cu(\mathbf{HL_2})Cl_2]$ (**2**), $[Cu_2(\mathbf{L_2})_2](ClO_4)_2$ (**3**) and $[Cu\mathbf{L_3}(HOCH_3)ClO_4]$ (**4**), complexes **1** and **3** were crystallographically analyzed. All the complexes showed catalysis on the hydroxylation of benzene to phenol involving hydroxyl radical mechanism as confirmed by the influence of radical scavengers such as TEMPO on the catalysis. Under optimized reaction conditions, the conversion of benzene was comparable (nearly 50%) whereas the reaction selectivity was not improved compared to our recent report with iron (III) complexes as catalysts.[19] But adding appropriate amount (100-fold of the catalyst) of TEMPO into the reaction could increase both the yield and selectivity of the reaction at the expense of the conversion of benzene (decrease by about one third).

2. Experimental

2.1 General procedures

Chemicals were purchased from Alfa Aesar and Sigma-Aldrich and used without further purification unless otherwise stated. Most of the organic solvents in this work were purified using drying agents. Elemental analyses were preformed on Elementar Vario MICRO. UV-vis absorption spectra were measured in the range of 200–700 nm on a Thermo Scientific EVOLUTION 201 in acetonitrile. ^{1}H and ^{13}C NMR spectra were recorded on Varian 400MHz in $CDCl_3$. Crystallographic data of complexes **1** and **3** were collected on a Bruker SMART CCD diffractometer with graphite-monochromated Mo–Kα radiation (λ = 0.71073 Å). The crystal structures were solved using direct methods in SHELXS program and refined by full-matrix least-squares routines, based on F^2, using the SHELXL package.[21] The crystallographic data of complexes **1** and **3** were deposited in the Cambridge Crystallographic Data Center (CCDC 1045737 for complex **1** and 1045738 for complex **3**). The hydroxylation of benzene by H_2O_2 as an oxidant was monitored and quantitatively analyzed by gas chromatography (Agilent 6890) with a packed column of Restek capillary SE-54. The temperature of the GC column was set at 60 ^oC for 1 min and then was programmed to 160 ^oC at the rate of 10 ^oC min^{-1}.

Electrochemistry was performed in a gas-tighten three-electrode system in which a vitreous carbon disk (Φ = 1 mm) was used as a working electrode, a carbon strip as counter electrode, and Ag / AgCl (inner reference solution: 0.45 mol L^{-1} $[N^nBu_4]BF_4$ + 0.05 mol L^{-1} $[N^nBu_4]Cl$ in dichloromethane) against which the potential of ferrocenium / ferrocene couple is 0.55 V in 0.5 mol L^{-1} $[N^nBu_4]BF_4$ in dichloromethane as described else where.[22, 23] Ferrocene was added as an internal standard and all potentials are quoted against ferrocenium / ferrocene couple (Fc^+ / Fc).

2.2 Catalytic assessment

2.2.1 General procedure

Benzene (0.9 mL, 10 mmol), acetonitrile (2.5 mL) and catalytic amount of the copper complex were placed into a reaction vessel equipped with cooling condenser and placed in an oil-bath. The reaction was heated at appropriate temperature for a period of time. When the reaction reached the specified temperature, appropriate amount of aqueous H_2O_2 (30 wt%) was slowly and carefully added in one-go. When the reaction was stopped and cooled, the volume of the reaction mixture was calibrated to 10 mL with CH_3CN in which there was an appropriate amount of toluene as an internal standard. To the calibrated reaction solution was added $MgSO_4$ (3 g) to remove the water in the reaction before being analyzed by gas chromatography. Quantitative analysis of both benzene and phenol was achieved by establishing their calibration curves with two linear equations under optimized conditions, $A_b/A_t = 0.0053\ W_b + 0.1266$ (R = 0.9986) and $A_p/A_t = 0.0034\ W_p - 0.1635$ (R = 0.9943) for benzene and phenol, respectively (Fig. S3), where A is the ratio of the peak areas of the analyte (benzene or phenol) and the internal standard toluene, W (mg) the mass of the analytes, the subscript b designated for benzene and p are and designated for phenol. The yield of phenol and benzene conversion was calculated as follows: phenol (mmol) / benzene initially used (mmol) × 100% and benzene–reacted (mmol) / benzene initially used (mmol) × 100%, respectively.

2.2.2 Optimizing the reaction conditions

In an orthogonal experimental design, four factors of reaction temperature, reaction time, catalyst dosage and amount of H_2O_2 with four levels were considered, Table 1.

Table 1 Factor levels used in the experiment.

Factor	A Reaction time (h)	B Temperature (^oC)	C Catalyst (mmol)	D[a] H_2O_2 (mL)
1	1	50	0.01	1
2	2	60	0.02	1.5
3	4	70	0.03	2
4	6	80	0.05	3

[a] Total volume of the reaction: 4.9 mL.

2.3 Synthesis

2.3.1 Preparation of 1-methyl-1H-imidazole-2-carbaldehyde (A). 1-Methylimidazole (4.1 mL, 50 mmol) was dissolved in dry THF (25 mL) under N_2 atmosphere, which was cooled to −78 ^oC and stirred for 10 min. To this solution was slowly added 20 mL of butyl-lithium (50 mmol, 2.5 mol L^{-1} in hexane). The reaction

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was stirred for 5 min before 7.5 mL (100 mmol) of dimethylformamide was added. The solution was further stirred for 1 h at −78 °C and then allowed to warm slowly to room temperature. Then, 25 mL HCl (12 mol L^{-1}) were added before another 1 h's stirring. The pH of the mixture was then adjusted to 10 with NaOH (aq., 40%) and extracted with dichloromethane (3 × 60 mL). All organic extracts were combined and dried with Na_2SO_4. After evaporation of the solvents, a yellow oily liquid (5.33 g, 97%) was collected by silica gel flash chromatography (eluent: ethyl acetate, EA). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.78 (s, 1H, CHO), 7.23 (s, 1H, Im), 7.07 (s, 1H, Im), 3.98 (s, 3H, CH_3).

2.3.2 Preparation of bis(pyridin-2-ylmethyl) amine (B). 2-Aminomethylpyridine (2.5 mL, 26 mmol) in methanol (20 mL) was dropwise added to 2-pyridinecarboxaldehyde (2.7 mL, 26 mmol) in methanol (40 mL). After being stirred overnight, $NaBH_4$ (2.42 g, 63.76 mmol) was slowly added and the mixture was further stirred for another day before being concentrated to dryness to give a residue to which water (60 mL) was added. The pH of the resultant solution was adjusted to 7 by HCl (2 mol L^{-1}) followed by extraction with CH_2Cl_2 (3 × 100 mL). The organic phases were combined and dried with $MgSO_4$. After evaporation of the solvents, a yellow oily liquid (3.32 g, 54%) was collected by silica gel flash chromatography (eluent: EA−EtOH−Et_3N = 5 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, J = 4.7 Hz, 2H, Py), 7.55 (t, J = 7.6 Hz, 2H, Py), 7.28 (s, 2H, Py), 7.14 – 6.98 (m, 2H, Py), 3.90 (s, 4H, CH_2), 2.86 (s, 1H, NH).

2.3.3 Preparation of 1-methyl-1H-imidazol-2-ylmethyl-(pyrid-2-ylmethyl)amine (C). 1-Methyl-1H-imidazole-2-carbaldehyde (**A**) (4.71 g, 42.8 mmol) in methanol (30 mL) was dropwise added to 2-aminomethylpyridine (4.62 g, 42.8 mmol) in methanol (50 mL). The mixture was stirred overnight and then $NaBH_4$ (2.28 g, 60 mmol) was added. The solution was further stirred for another day before being concentrated to dryness. The resultant residue was dissolved in water (30 mL) and extracted with dichloromethane (3 × 40 mL). The organic phases were combined and dried with $MgSO_4$. After evaporation of the solvents, a light yellow oily liquid (3.45 g, 40%) was attained by column chromatography (eluent: EA−EtOH−Et_3N = 5 : 1: 0.1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (d, J = 4.3 Hz, 1H, Py), 7.56 (td, J = 7.7, 1.7 Hz, 1H，Py), 7.25 (t, J = 5.8 Hz, 1H, Py), 7.08 (dd, J = 6.9, 5.5 Hz, 1H, Py), 6.84 (s, 1H, Im), 6.73 (s, 1H, Im), 3.86 (s, 2H, CH_2), 3.82 (s, 2H, CH_2), 3.58 (s, 3H, CH_3), 3.07 (s, 1H, NH).

2.3.4 Preparation of ligand L_1. To a solution of bis(pyridin-2-ylmethyl) amine (**B**) (1.90 g, 10 mmol) in THF (60 mL) was added K_2CO_3 (5.52 g, 40 mmol) and propargyl bromide (0.8 mL, 10 mmol). After being stirred at room temperature for 6 h, the reaction was filtered. After evaporation of the solvents, a yellow oily liquid (1.85 g, 78%) was collected by column chromatography (eluent: EA−EtOH−Et_3N = 5 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.7 Hz, 2H, Py), 7.68 (td, *J* = 7.6, 1.6 Hz, 2H, Py), 7.54 (d, *J* = 7.8 Hz, 2H, Py), 7.21 – 7.16 (m, 2H, Py), 3.94 (s, 4H,CH_2), 3.45 (d, *J* = 2.3 Hz, 2H, CH_2), 2.32 (t, *J* = 2.3 Hz, 1H, CH).

2.3.5 Preparation of ligands HL_2 and HL_3. To a solution of salicylaldehyde (1.05 g, 8.6 mmol) in methanol (25 mL) was added 1-methyl-1H-imidazol-2-ylmethyl-(pyrid-2-ylmethyl) amine (1.73 g, 8.6 mmol) and a small amount of acetic acid. And then sodium triacetoxyborohydride (2.12 g, 10 mmol) in methanol (5 mL) was dropwise added to the resulting solution under stirring. After the solution was stirred for 2 days at room temperature, it was acidified by adding HCl (2 mol L^{-1}) and then evaporated to dryness under reduced pressure. The residue was dissolved in saturated aqueous Na_2CO_3 solution (25 mL) and extracted with $CHCl_3$ (3 × 50 mL). The combined extracts were dried over anhydrous Na_2SO_4 and filtered. A light yellow oily liquid (1.14 g, 43%) was collected by column chromatography (eluent: EA−EtOH−Et_3N = 5 : 1 : 0.1). ^{1}H NMR (400 MHz, $CDCl_3$): δ10.90 (s, 1H, OH), 8.54 (d, J = 4.8 Hz, 1H, Py), 7.60 (td, J = 7.7, 1.6 Hz, 1H, Py), 7.21 – 7.13 (m, 3H, 2Py, Ph), 7.06 (d, J = 7.4 Hz, 1H, Ph), 6.91 – 6.86 (m, 2H, Ph, Im), 6.76 (dd, J = 7.3, 6.8 Hz, 1H, Ph), 6.71 (s, 1H, Im), 3.85 (s, 2H, CH_2), 3.72 (s, 4H, $2CH_2$), 3.38 (s, 3H, CH_3).

Ligand HL_3 as a white solid (2.73 g, 87%) was analogously synthesized by using the procedure employed for the preparation of HL_2 but using 3-*tert*-butyl-2-hydroxybenzaldehyde as the aldehyde and sodium cyanoborohydride as the reducing agent. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.78 (s, 1H, OH), 8.53 (d, J = 4.8 Hz, 1H, Py), 7.56 (td, J = 7.7, 1.6 Hz, 1H, Py), 7.22 – 7.16 (m, 1H, Py), 7.15 – 7.07 (m, 2H, Py), 6.91 (d, J = 6.5 Hz, 1H, Py), 6.82 (d, J = 0.9 Hz, 1H, Im), 6.68 (dd, J = 14.3, 6.8 Hz, 2H, Py, Im), 3.81 (s, 2H, CH_2), 3.71 (s, 4H, $2CH_2$), 3.32 (s, 3H, CH_3), 1.41 (s, 9H, $3CH_3$).

2.3.6 Preparation of complexes 1 and 2. Complex **1** was prepared by the reaction of a solution of $CuCl_2{\cdot}2H_2O$ (0.34 g, 2.0 mmol) in methanol (2 mL) with ligand L_1 (0.47 g, 2.0 mmol) in methanol (3 mL). The reaction turned blue and blue precipitate formed gradually. After being stirred at room temperature for 1 h, the precipitate (0.64 g, 83%) was collected by filtration, washed successively with small amounts of methanol, diethyl ether (5 × 50 mL), and then dried in *vacuo*. Blue crystals of complex **1** were obtained by recrystallization from methanol / diethyl ether. Elemental analysis for complex **1** ($C_{15}H_{15}Cl_2CuN_3{\cdot}H_2O$, FW = 388.00), calc. (%): C, 46.22; H, 4.40; N, 10.78; Found (%): C, 46.32; H, 4.31; N, 10.37.

Complex **2** (0.96 g, 82%) was synthesized by using the same procedure employed for the preparation of complex **1** by replacing the ligand with ligand HL_2. Elemental analysis for complex **2** ($C_{19}H_{24}Cl_2CuN_4O_2{\cdot}H_2O$, FW = 491.07), calc. (%): C, 46.30; H, 5.32; N, 11.37. Found (%): C, 46.08; H, 4.94; N, 11.90.

2.3.7 Preparation of complexes 3 and 4. Complex **3** was prepared by the reaction of a solution of $Cu(ClO_4)_2{\cdot}6H_2O$ (0.75 g, 2.0 mmol) in methanol (2 mL) with ligand HL_2 (0.62 g, 2.0 mmol) in methanol (3 mL) in the presence of one equivalent potassium hydroxide (KOH). The solution was stirred for 1 h to obtain a light blue precipitate (0.91 g, 94%), which was collected by filtration, washed successively with small amounts of methanol, diethyl ether (5 × 50 mL), and dried in *vacuo*. Blue crystals of complex **3** were obtained by recrystallization from methanol / dichloromethane. Elemental analysis for complex **3** ($C_{36}H_{38}N_8O_{10}Cu_2Cl_2{\cdot}CH_2Cl_2$, FW = 1022.02, calc. (%): C, 43.86; H, 4.16; N, 10.77. Found (%): C, 43.88; H, 3.76; N, 10.87.

Complex **4** (0.84 g, 70%) was synthesized by using the same procedure employed for the preparation of complex **3** by using ligand HL_3. Elemental analysis for complex **4** ($C_{23}H_{31}N_4O_6CuCl{\cdot}CH_2Cl_2$, FW = 641.08), calc. (%): C, 44.80; H,

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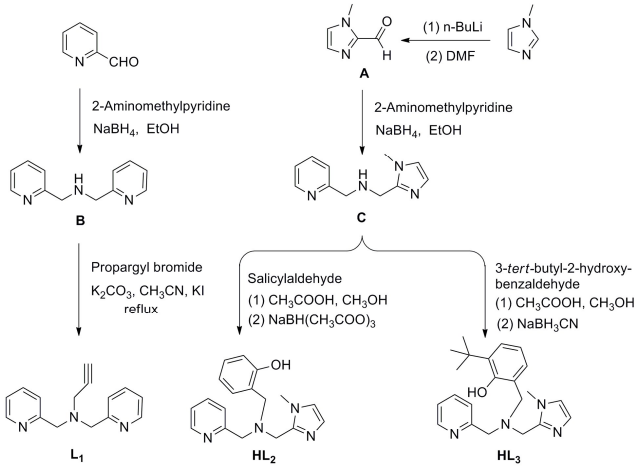
5.17; N, 8.71. Found (%): C, 44.43; H, 5.99; N, 8.98.

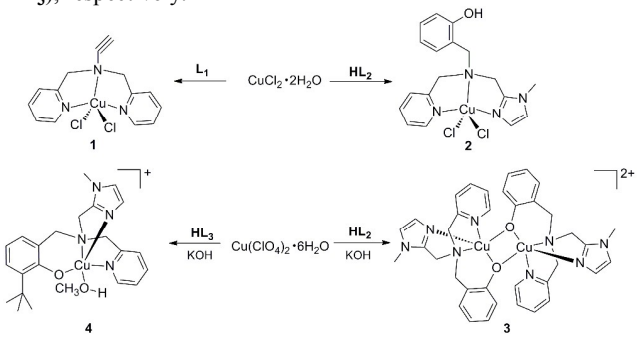
3. Results and discussion

3.1 Synthesis of ligands L_1, HL_2, HL_3 and their copper complexes 1–4



Scheme 2 Synthesis of ligands L_1, HL_2 and HL_3.

The synthesis of the ligands are shown in Scheme 2. Ligand L_1 was prepared using the procedure as we reported recently.[19] Ligands HL_2 and HL_3 were analogously made using Mannich reaction. The first aldehyde (**A**) was prepared following the literature procedure.[24] The aldehyde reacted further with 2-aminomethylpyridine to form the secondary amine (**C**) which reacted with salicylaldehyde and 3-*tert*-butyl-2-hydroxybenzaldehyde to lead to the desired ligands (HL_2 and HL_3), respectively.



Scheme 3 Synthesis of copper complexes **1**–**4**.

The synthetic routes of the four copper complexes are shown in Scheme 3. Treatment of $CuCl_2{\cdot}2H_2O$ with ligands L_1 and HL_2 led to the formation of mono nuclear complexes **1** and **2**, respectively. In complex **2**, the phenol group is pendant without being deprotonated. Deliberately deprotonating the phenol of ligand HL_2 in reaction with $Cu(ClO_4)_2{\cdot}6H_2O$ led to the dinuclear complex **3** in which the phenolates bridged the two copper (II) centre together. This came as no surprise since a phenolate is found a good bridging ligand.[25, 26] To prevent the reaction from forming a dinuclear complex, a common strategy is to introduce a bulky group *ortho* to the phenol group, which could hinder the dimerisation. To this end, ligand HL_3 was synthesized. Indeed, its reaction with $Cu(ClO_4)_2{\cdot}6H_2O$ gave supposedly a mononuclear complex **4**. Without crystal structure, its composition was established using microanalysis, conductivity and electrochemistry (*vide infra*). It is well known that in a specified organic solvent, the charge number of a transition metal complex correlates well with its conductivity.[27] In acetonitrile the conductivity of complex **4** was 125.4 μs cm^{-1} (Table S1), which is within the conductivity range of mono-charged complex ions (92–199 μs cm^{-1}). Thus, in addition to its microanalysis, complex **4** is tentatively assigned to a mono-cation salt. All the reactions gave an excellent yield (over 80 %).

3.2 Single-crystal X-ray diffraction

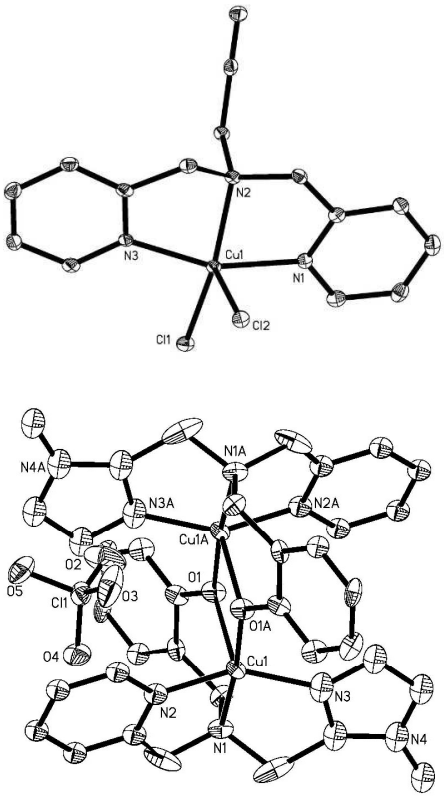


Fig. 1 ORTEP view of complexes **1** (top) and **3** (bottom) with 30% probability level ellipsoids. The hydrogen atoms are omitted for clarity.

The crystals of complexes **1** and **3** suitable for X-ray single crystal diffraction analysis were grown from methanol solution into which the vapor of diethyl ether or dichloromethane was diffused. Their structures are shown in Fig. 1 and their crystallographic data and selected bonding parameters are tabulated in Table 2 and Table 3, respectively. Both complexes **1** and **3** crystallized in monoclinic crystal system with the same space group. Complex **1** is mononuclear and the central Cu (II) is pentacoordinated with a distorted square pyramid with "$N_1N_2N_3Cl_1$" as the basal plane. But the Cu (II) ion is out of the plane by about 20°. Complex **3** contains a dinuclear copper core

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with intermetallic separation of 3.13 Å, suggesting no bonding interaction between them. Each Cu (II) is doubly bridged by an endogenous ligand-derived phenoxide oxygen-atom (O1) and three nitrogen atoms (N1, N2 and N3) to construct the pentacoordination with "N_3O_2" donor atoms. The counter anion (ClO_4^-) have no interaction with the dicationic portion of the molecule.

3.3 Redox behaviours of complexes 1–4

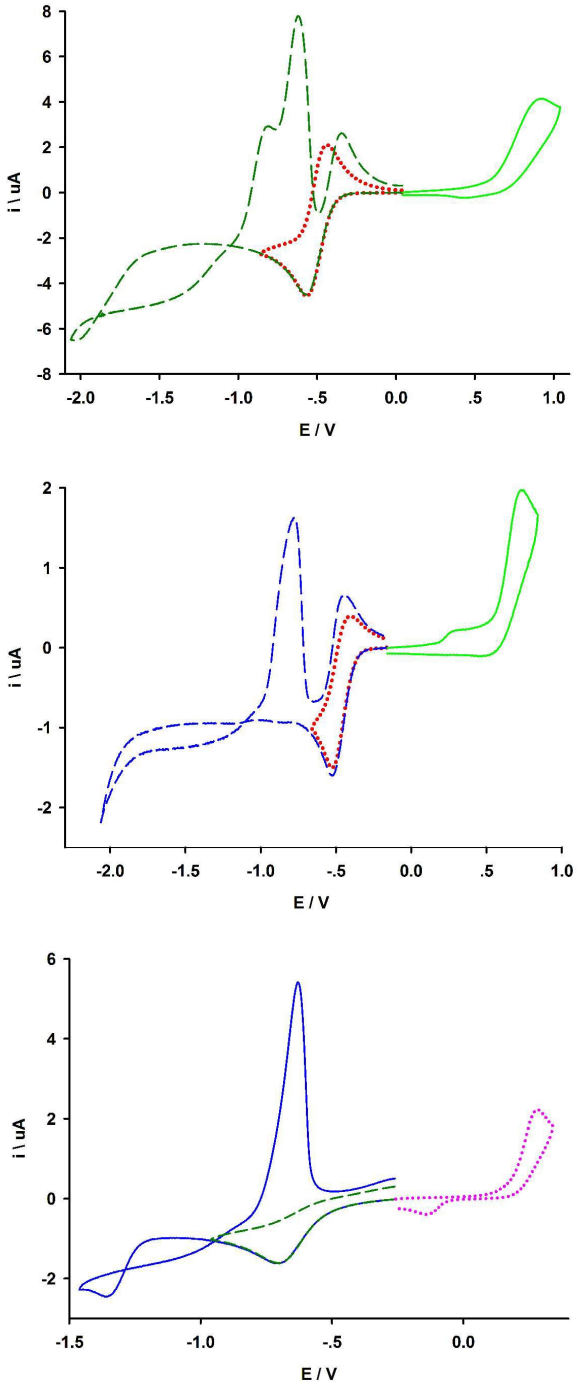

Fig. 2 Cyclic voltammograms of complexes **1** (top, 3.2 mmol L^{-1}), **2** (middle, 3.2 mmol L^{-1}) and **4** (bottom, 3.2 mmol L^{-1}) in 0.1 mol L^{-1} $[N^nBu_4]BF_4$–CH_3CN under Ar atmosphere (298 K, scanning rate = 100 mV s^{-1}).

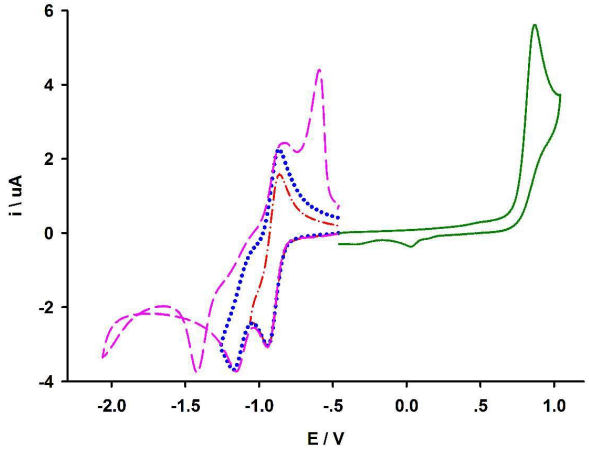

Fig. 3 Cyclic voltammograms of complex **3** (3.2 mmol L^{-1}) in 0.1 mol L^{-1} $[N^nBu_4]BF_4$–CH_3CN under Ar atmosphere (298 K, scanning rate = 100 mV s^{-1}).

In the hydroxylation of benzene with H_2O_2 as the oxidant, most likely, the metal complexes activate first the oxidant to produce either hydroxyl radical or active oxo-containing species rather than the substrate. In the activation of the oxidant, its binding to the metal centre is essential. Thus, it is anticipated that its binding to the metal centre would be affected by the electron density on the metal centre and thus the activation of the oxidant. Therefore, the electrochemical behaviours of the complexes ought to be informative of how the electronic property of the complexes correlates to their catalysis. Recently, we reported the same reaction catalyzed by Fe(III) complexes.[19] Our study indicated that the more negative the potential of the Fe(III) complexes, the better the catalytic performance. In the case of Fe(III) complexes, the correlation has been clear. It is interesting to know whether such a correlation applies in these copper complexes.

To do so, their electrochemistry was examined. In the reduction of complexes **1**, **2** and **4** (Fig. 2), the first process is unambiguously assigned to the reduction of Cu(II) → Cu(I). When the potential scanned further to the negative region, the second process was observed, which was well below −2.0 V. The followed returning scanning produced a sharp oxidation peak between −0.7 V and −0.8 V. This is a typical anodic copper-stripping process. Complex **4** showed a difference in the reversibility of the Cu(II) → Cu(I) process. As indicated by the deduction of its formula, in addition to the four coordinating atoms, a CH_3OH molecule might ligate to the metal centre to meet the fifth coordination. The binding of the methanol molecule is usually weak and prone to dissociation upon reduction, which caused the irreversibility. For complex **3**, one more quasi-reversible reduction following closely the first Cu(II) → Cu(I) reduction was observed (Fig. 3). It could not be the successive reduction from Cu(I) to Cu(0) as not only is it too close to the first reduction, but also the characteristic anodic copper-stripping was absent. It may also be responsible for a by-product from the first reduction although it is highly unlikely

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since the first process is reversible. Its electrochemistry at various scanning rates and low temperature excluded also this possibility (Fig. S2). By considering the di-nuclear nature, the second reduction process is tentatively assigned to the reduction of Cu(II) → Cu(I) of the other copper centre.

3.4. Catalytic hydroxylation of benzene to phenol

Under optimized reaction conditions (Fig. S4, Tables S2 and S3), the catalytic performances of these copper complexes were investigated and the results are summarized in Table 4. As mentioned earlier, we observed recently that the catalytic performances of the iron (III) complexes correlate to their reduction potentials.[19] As revealed by the results shown in Table 4, such a correlation exists also, but unlike the iron (III) complexes which possess roughly a linear correlation, these copper (II) complexes did not show a good linear correlation (Fig. 4) due to lacking of sufficient data. Among the complexes, complex **4** is of the most negative reduction potential and exhibited marginally better catalytic performance (~10%) in the conversion (Fig. 4) compared to the iron (III) analogues.[19] But the phenol yield or selectivity deteriorated by nearly 50%. This may be attributed to the radical mechanism because the radical generated catalytically by the copper (II) complexes made no discrimination in the oxidation of both benzene and phenol. Furthermore, phenol is more prone than benzene to oxidation.

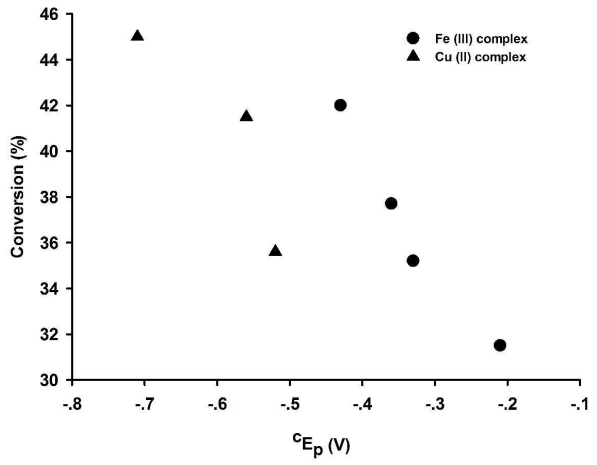

Fig. 4 The correlations of reduction potentials to the conversion of benzene.

To further confirm the radical mechanism, we used three radical scavengers, which are ethanol, TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) and DMPO (5,5-dimethyl-1-pyrroline N-oxide), Table 5. The addition of these scavengers decreased steadily the reaction conversion, which supported the involvement of a radical in the catalysis. It was reported that a linear correlation of the ratio of the yield with the presence of the scavenger ethanol over the yield without the scavenger to the concentration of the added ethanol could be observed if the catalysis involves a hydroxyl radical.[28, 29] The data given in Table 5 shows indeed such a linear plot (Fig. S5, R = 0.9937). As illustrated in Table 5, all the scavengers led to steady decrease in conversion and enhancement in selectivity. In general, the yield decreased monotonically except for TEMPO (Table 5). Such variations can be attributed to the reduction in the concentration of hydroxyl radical. But the influence of TEMPO on the catalysis was somewhat exceptional as the reaction yield underwent first increase and then decrease with the addition of the scavenger, which is contrary to the other two radical scavengers (Table 5 and Fig. 5). As shown by the data in Table 5, under the same condition, TEMPO is probably the most efficient radical scavenger and the concentration of hydroxyl radical decreased more rapidly compared to the other two. Thus, at the early stage, the over-oxidation of the phenol was much eased due to the decrease in the concentration of the radical compared to the other two scavengers. Further addition of the scavenger decreased continuously the radical concentration and then the reaction yield went down as those of ethanol and DMPO.

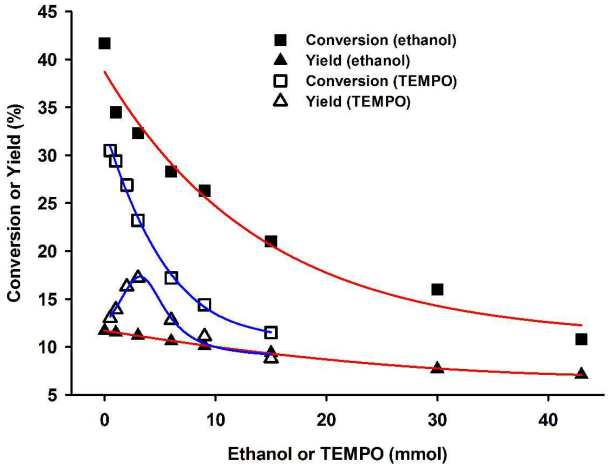

Fig. 5 The influence of ethanol and TEMPO on the conversion of benzene and the yield of phenol.

4. Conclusions

In summary, we have described the synthesis and characterization of four copper (II) complexes **1**–**4** derived from three multidentate ligands. Of the four complexes, complex **3** is a dimer. These complexes catalyze the direct hydroxylation of benzene. The correlation between reduction potential and catalytic performance as we reported previously[19] exists also among the copper (II) complexes. Furthermore, the comparison between the iron (III) and copper (II) complexes suggests that the catalytic performance of a transition metal complex is profoundly affected by both its reduction potential and the metal itself. It seems that radical mechanism applies for both metals when H_2O_2 is employed as an oxidant. The radical is most likely a hydroxyl radical. The radical mechanism may explain why the reaction selectivity is poor as the product phenol could be more readily subject to oxidation by the radical compared to the precursor benzene. It is clearly that for a specific metal, the electronic property of its complexes has to be tuned in such a way that the reduction potentials shift negatively, to benefit the generation of hydroxyl radical. How to suppress the over-oxidation of the product phenol to improve the selectivity/yield remains a huge challenge in the homogeneous catalytic hydroxylation of

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benzene!

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Notes and references

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Table 2 Crystallographic details and refinement data for complexes **1** and **3**.

Complex	**1**	**3**
Empirical formula	$C_{15}H_{17}Cl_2Cu\,N_3O$	$C_{36}H_{38}Cl_2Cu_2N_8O_{10}$
F_w	389.76	940.74
Crystal system	Monoclinic	Monoclinic
space group	P21/c	P21/c
a/Å	9.268(4)	12.006(5)
b/Å	13.526(6)	9.927(4)
c/Å	13.154(6)	17.447(6)
α / (°)	90	90
β / (°)	97.941 (6)	116.68(2)
γ / (°)	90	90
V, Å^3	1633.1(12)	1858.0(13)
Z	4	2
D_c / (g/cm^{-3})	1.585	1.681
F(000)	796	964
Reflections collected(R_{int})	12307 (0.0646)	12925 (0.0785)
Reflections independent	3206	3265
Goodness-of-fit on F^2	1.052	1.169

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$R_1[I > 2\sigma(I)]$	0.0454	0.1071
wR_2 (all data)	0.1176	0.2563

Table 3 Selected bond distances (Å) and angles (°) for complexes **1** and **3**.

1			
Cu(1)-N(1)	2.007(3)	Cu(1)-Cl(1)	2.2576(11)
Cu(1)-N(3)	2.017(3)	Cu(1)-Cl(2)	2.4912(13)
Cu(1)-N(2)	2.041(3)		
N(1)-Cu(1)-N(3)	160.14(11)	N(2)-Cu(1)-Cl(1)	157.67(7)
N(1)-Cu(1)-N(2)	80.78(11)	N(1)-Cu(1)-Cl(2)	92.30(7)
N(3)-Cu(1)-N(2)	80.62(11)	N(3)-Cu(1)-Cl(2)	96.29(7)
N(1)-Cu(1)-Cl(1)	97.41(9)	N(2)-Cu(1)-Cl(2)	95.33(7)
N(3)-Cu(1)-Cl(1)	97.14(9)	Cl(1)-Cu(1)-Cl(2)	107.00(3)
3			
Cu(1)-O(1)	2.212(7)	Cu(1)-N(2)	1.973(6)
Cu(1)-O(1A)	1.926(8)	Cu(1)-N(3)	1.954(9)
Cu(1)-N(1)	2.058(9)		
O(1)-Cu(1)-N(1)	92.6(3)	O(1A)-Cu(1)-N(1)	173.4(3)
O(1)-Cu(1)-N(2)	98.0(3)	O(1)-Cu(1)-O(1A)	82.2(3)
O(1)-Cu(1)-N(3)	105.0(4)	N(1)-Cu(1)-N(2)	82.5(3)
O(1A)-Cu(1)-N(3)	102.0(4)	N(1)-Cu(1)-N(3)	83.2(4)
O(1A)-Cu(1)-N(2)	94.2(3)	N(2)-Cu(1)-N(3)	153.4(4)

Table 4 Redox potentials of the complexes and their catalytic performances.

	$^{c}E_p$ [a] (V)	$E_{1/2}$ [b] (V)	$^{a}E_p$ [c] (V)	Conversion (%)	Yield (%)	TON	TOF (h^{-1})
Complex **1**	-0.56	-0.51	0.90	41.5 ± 0.2	11.0 ± 0.8	36.7	9.2
Complex **2**	-0.52	-0.46	0.73	35.6 ± 1.0	11.3 ± 0.5	37.7	9.4
Complex **3**	-0.94 -1.17[d]	-0.90	0.86	47.7 ± 1.3	11.9 ± 0.5	79.3	19.8
Complex **4**	-0.71	—	0.28	45.0 ± 1.8	14.6 ± 1.0	48.7	12.2

[a] Cu(II)→Cu(I) reduction peak potential.
[b] Half-wave potential where applicable.
[c] Oxidation peak potential.
[d] The second Cu(II)→Cu(I) reduction peak potential.

Table 5 The influence of radical scavengers on the catalytic performances.

Entry	Radical scavenger	Conversion (%)	Yield (%)	Selectivity (%)
1[a]	—	41.7	11.7	28.1
2	1 mmol Ethanol	34.5	11.5	33.3
3	3 mmol Ethanol	32.3	11.2	34.8
4	6 mmol Ethanol	28.3	10.6	37.5
5	9 mmol Ethanol	26.3	10.1	38.4
6	15 mmol Ethanol	21.0	9.4	44.8
7	30 mmol Ethanol	16.0	7.7	48.1
8[b]	43 mmol Ethanol	10.8	7.1	65.7
9[c]	1.0 mmol TEMPO	0	0	—
10[d]	1.0 mmol TEMPO	0	0	—
11[e]	1.0 mmol TEMPO	0	0	—

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12	0.5 mmol TEMPO	30.5	13.0	46.2
13	1.0 mmol TEMPO	29.4	13.9	47.3
14	2.0 mmol TEMPO	26.9	16.3	60.6
15	3.0 mmol TEMPO	23.2	17.2	74.1
16	6.0 mmol TEMPO	17.2	12.8	74.4
17	9.0 mmol TEMPO	14.4	11.1	77.1
18	15.0 mmol TEMPO	11.5	8.8	76.5
19	1.0 mmol DMPO	34.4	11.6	33.7
20	15.0 mmol DMPO	27.7	10.6	38.3

[a] Reaction conditions: complex **1** (0.03 mmol), benzene (0.9 mL, 10 mmol), H_2O_2 (1.5 mL, 15 mmol), acetonitrile as solvent (2.5 mL), temp = 80 ^oC, time = 4 h.
[b] Using ethanol as solvent (2.5 mL).
[c] Under the standard conditions without complex **1**.
[d] Under the standard conditions without complex **1** and irradiation for 4h.
[e] Under the standard conditions without H_2O_2.